

Applicants: Jeffrey Sterling et al.

Serial No.: Not Yet Known

Filed : Herewith

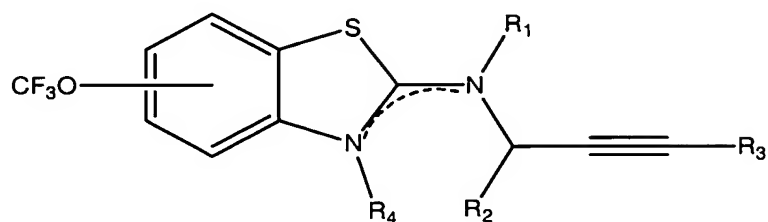
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Amendments to the Claims

Please cancel claims 69-73 without prejudice to applicants' rights to pursue the subject matter of these claims in this or a related application.

Please amend claims 8-11, 14 and 41, and add new claim 74 under the provisions of 37 C.F.R. §1.121, as set forth in the Federal Register on June 30, 2003 as follows:

1. (Original) A compound having the structure:



wherein

R₁ is present or absent, and when present is H, C₁-C₆ alkyl, C₁-C₆ alkynyl, $-(CH_2)_yS(CH_2)_xCH_3$, C₁-C₆ aminoalkyl, C₁-C₆ hydroxyalkyl or $-(CH_2)_nC(=O)(C_6H_4)(CH_2)R_2$;

R₂ is H or C₁-C₄ alkyl;

R₃ is H or C₁-C₄ alkyl;

R₄ is present or absent, and when present is H, C₁-C₆ alkyl, C₁-C₆ alkynyl, $-(CH_2)_yS(CH_2)_xCH_3$, C₁-C₆ aminoalkyl, C₁-C₆ hydroxyalkyl or $-(CH_2)_nC(=O)(C_6H_4)(CH_2)R_2$;

wherein n is an integer from 1-6;

wherein x is 0 or an integer from 1-5 and

y is an integer from 1-5, such that x+y<6;

at least one of R₁ or R₄ is present;

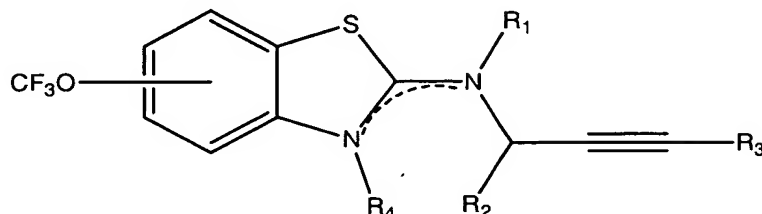
the dashed line represents a bond between one of the nitrogen atoms and the intervening carbon atom; and

the compound is charged when both R₁ and R₄ are present,

or a specific enantiomer thereof or a pharmaceutically acceptable salt thereof.

2. (Original) The compound of claim 1, wherein at least one of R₁ or R₄ is $-(CH_2)_nC(=O)(C_6H_4)(CH_2)R_2$.

3. (Original) The compound of claim 1, wherein at least one of R_1 and R_4 is $-(CH_2)_yS(CH_2)_xCH_3$.
4. (Original) The compound of claim 1, having the structure:



wherein

R_1 is present or absent, and when present is H or C₁-C₄ alkyl;

R_2 is H or C₁-C₄ alkyl;

R_3 is H or C₁-C₄ alkyl;

R_4 is present or absent, and when present is H or C₁-C₄ alkyl;

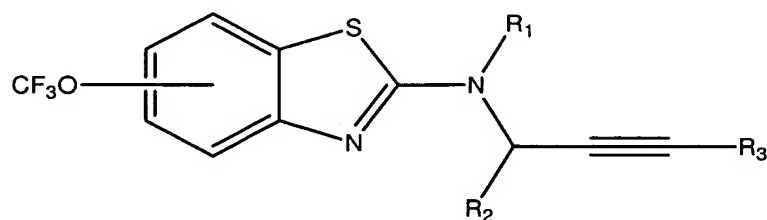
at least one of R_1 or R_4 is present;

the dashed line represents a bond between one of the nitrogen atoms and the intervening carbon atom; and

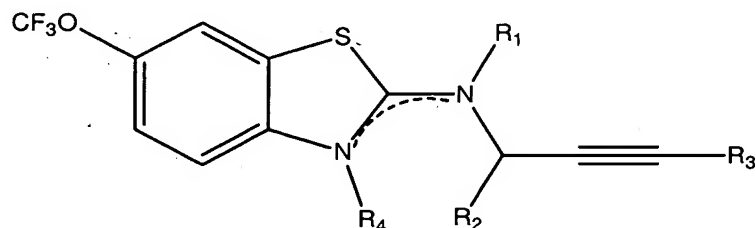
the compound is charged when both R_1 and R_4 are present,

or a specific enantiomer thereof or a pharmaceutically acceptable salt thereof.

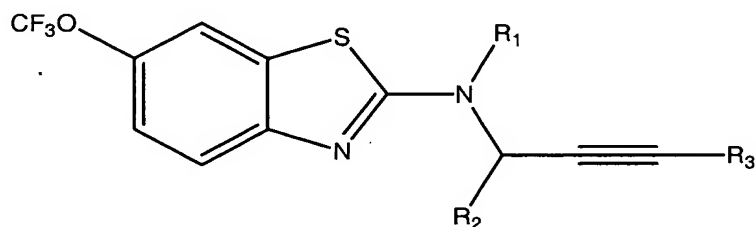
5. (Original) The compound of claim 4, having the structure:



6. (Original) The compound of claim 4, having the structure:



7. (Original) The compound of claim 4, having the structure:

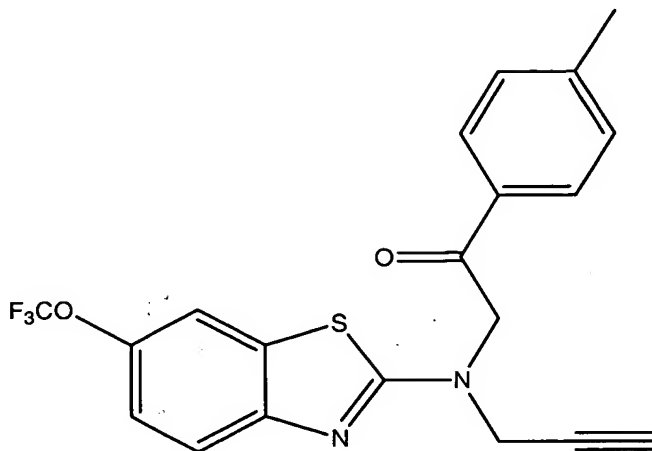


8. (Currently amended) The compound of ~~claim 4, 5, 6 or 7~~
claim 4, wherein at least one of R₁, R₂ and R₃ is C₁-C₄
alkyl.
9. (Currently amended) The compound of ~~claim 4 or 6~~, claim
4, wherein R₁ is absent and R₄ is present.

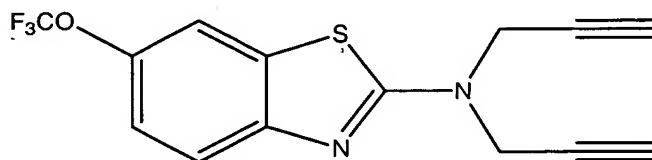
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10. (Currently amended) The compound of ~~claim 4, 5, 6 or 7~~
claim 4, wherein the chiral carbon is in the R
configuration.
11. (Currently amended) The compound of ~~claim 4, 5, 6 or 7~~
claim 4, wherein the chiral carbon is in the S
configuration.
12. (Original) The compound of claim 9, wherein R₁ is absent
and R₄ is methyl.
13. (Original) The compound of claim 7, wherein
R₁ is H or methyl;
R₂ is H or methyl;
R₃ is H or methyl,
or a pharmaceutically acceptable salt thereof.
14. (Currently amended) The pharmaceutically acceptable salt
of the compound of ~~any one of claims 1-13~~ claim 1,
wherein the salt is the chloride, mesylate, maleate,
fumarate, tartarate, hydrochloride, hydrobromide,
esylate, p-toluenesulfonate, benzoate, acetate, phosphate
or sulfate salt.

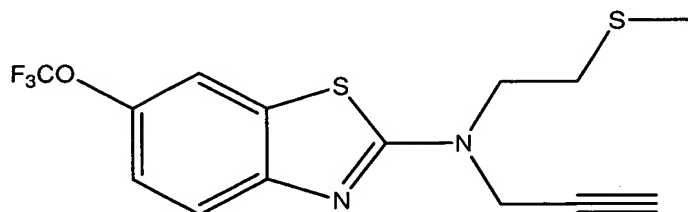
15. (Original) The compound of claim 2 having the structure:



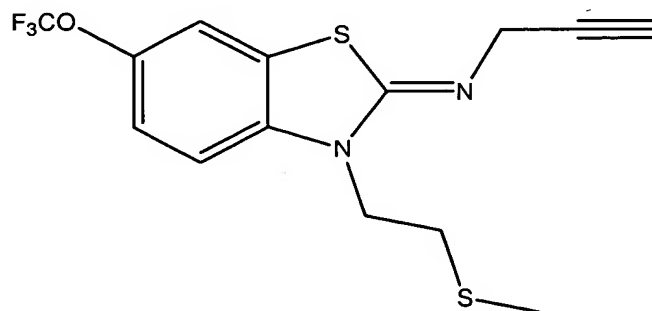
16. (Original) The compound of claim 1 having the structure:



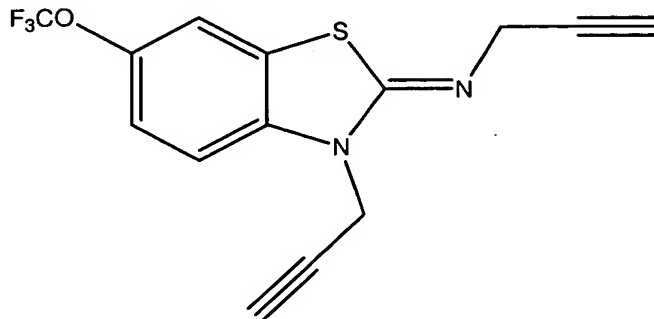
17. (Original) The compound of claim 3 having the structure:



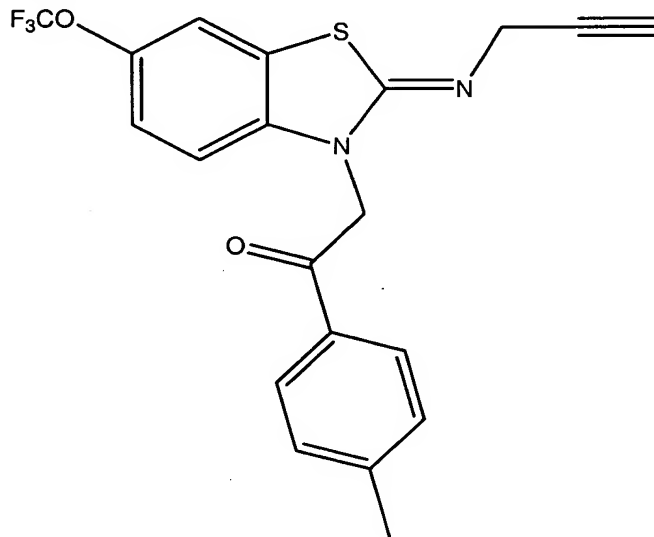
18. (Original) The compound of claim 3 having the structure:



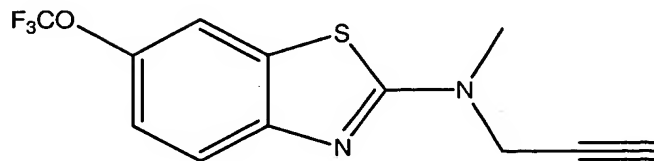
19. (Original) The compound of claim 1 having the structure:



20. (Original) The compound of claim 2 having the structure:

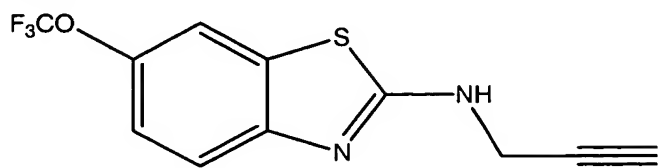


21. (Original) The compound of claim 7, having the structure:



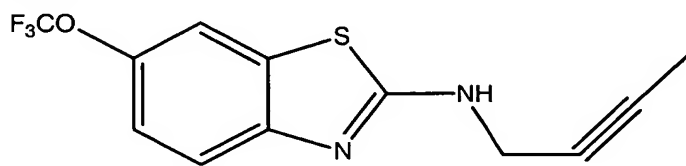
22. (Original) The hydrochloride salt of the compound of claim 21.

23. (Original) The compound of claim 7, having the structure:



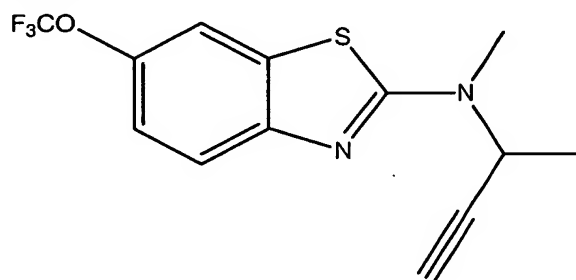
24. (Original) The hydrochloride salt of the compound of claim 23.

25. (Original) The compound of claim 7, having the structure:



26. (Original) The hydrochloride salt of the compound of claim 25.

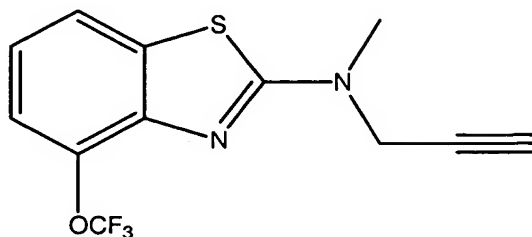
27. (Original) The compound of claim 7, having the structure:



28. (Original) The hydrochloride salt of the compound of claim 27.

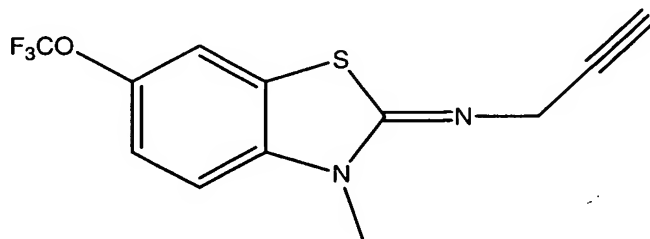
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29. (Original) The compound of claim 5, having the structure:



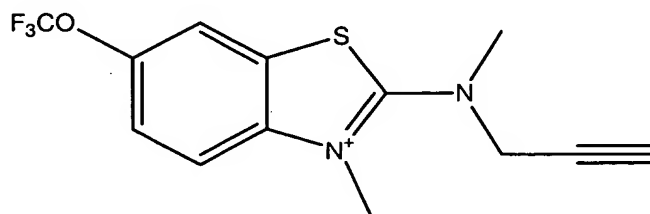
30. (Original) The hydrochloride salt of the compound of claim 29.

31. (Original) The compound of claim 6, having the structure:



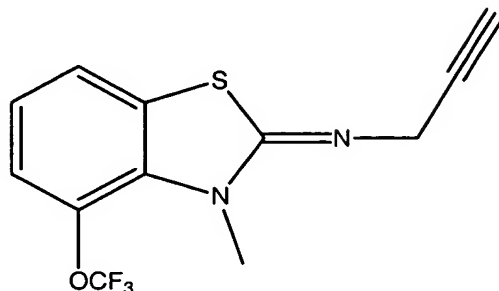
32. (Original) The hydrochloride salt of the compound of claim 31.

33. (Original) The compound of claim 4, having the structure:



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34. (Original) The compound of claim 4, having the structure:



35. (Original) A method for treating a subject afflicted with a neurologic disorder comprising administering to the subject a therapeutically effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof, so as to thereby treat the neurologic disorder in the subject.
36. (Original) The method of claim 35, wherein the neurologic disorder is Parkinson's Disease, Alzheimer's Disease, amyotrophic lateral sclerosis, stroke, a neuromuscular disorder, schizophrenia, cerebral infarction, head trauma, glaucoma, facialis or Huntington's Disease.
37. (Original) The method of claim 35, wherein the therapeutically effective amount is from about 1 to about 1000 mg/day.
38. (Original) A method for treating a subject afflicted with multiple sclerosis comprising administering to the subject a therapeutically effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof so as to thereby treat multiple sclerosis in the subject.

39. (Original) The method of claim 38, further comprising administering to the subject a therapeutically effective amount of levodopa, glatiramer acetate, interferon beta-1b, interferon beta-1a, steroids or Mitoxantrone.
40. (Original) The method of claim 38, wherein the therapeutically effective amount is from about 1 to about 1000 mg/day.
41. (Currently amended) The method of claim 35 ~~or 38~~ wherein the therapeutically effective amount of the compound is administered by injection, systemically, orally or nasally.
42. (Original) A method for destroying or inhibiting the proliferation of microbes or fungus which comprises contacting the microbes or fungus with a composition comprising the compound of claim 1 and an acceptable carrier.
43. (Original) A pharmaceutical composition comprising the compound of claim 1 and a pharmaceutically acceptable carrier.
44. (Original) The pharmaceutical composition of claim 43, further comprising a therapeutically effective amount of levodopa, glatiramer acetate, interferon beta-1b, interferon beta-1a, steroids or Mitoxantrone.
45. (Original) The pharmaceutical composition of claim 43, further comprising a therapeutically effective amount of glatiramer acetate.

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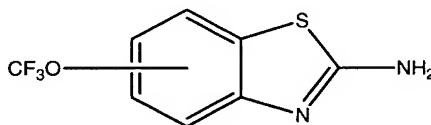
46. (Original) A process for the manufacture of a pharmaceutical composition comprising admixing the compound of claim 1 with a pharmaceutically acceptable carrier.

47. (Original) A packaged pharmaceutical composition for treating a neurologic disorder in a subject comprising:

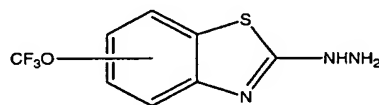
- (a) the pharmaceutical composition of claim 43; and
- (b) instructions for using the composition for treating the neurologic disorder in the subject.

48. (Original) A process of manufacturing the compound of claim 4 comprising the steps of:

- (a) reacting



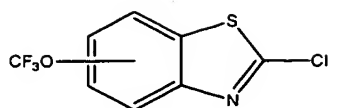
under suitable conditions with an amine exchanging agent in the presence of solvent to provide:



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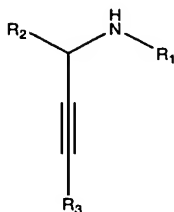
;

- (b) treating 2 with a chlorinating agent to provide

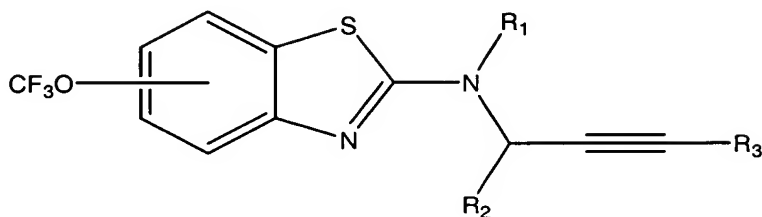


3 ;

(c) reacting 3 with



to provide



wherein

R₁ is present or absent, and when present is H or C₁-C₄ alkyl;

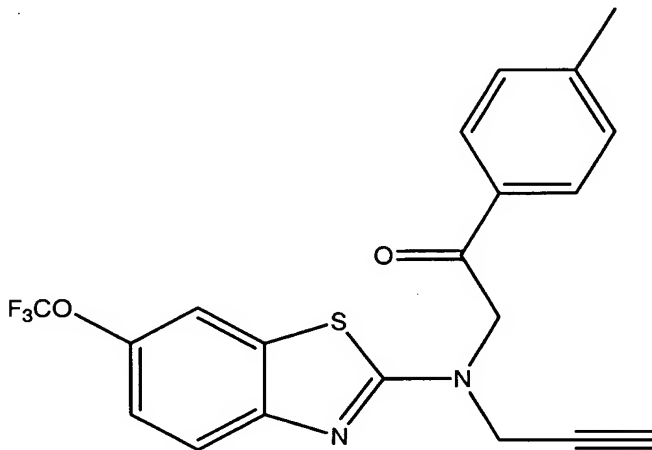
R₂ is H or C₁-C₄ alkyl;

R₃ is H or C₁-C₄ alkyl; and

(d) optionally alkylating the product of step (c), wherein R₁ is H, to provide the compound.

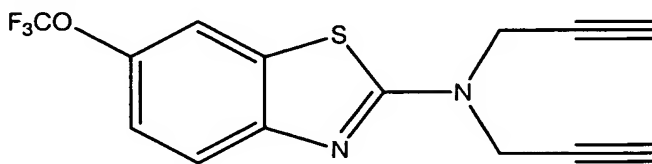
49. (Original) The process of claim 48, further comprising reacting the product of step (c), wherein R₁, R₂ and R₃

are each H, with 2-bromo-4'-methylacetophenone in a polar solvent in the presence of a base to produce a compound having the structure:



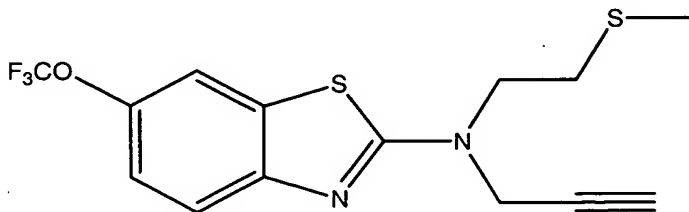
50. (Original) The process of claim 49, wherein the polar solvent is acetonitrile and the base is potassium carbonate.

51. (Original) The process of claim 48, further comprising reacting the product of step (c), wherein R_1 , R_2 and R_3 are each H, with propargyl bromide in a polar solvent in the presence of a base to produce a compound having the structure:

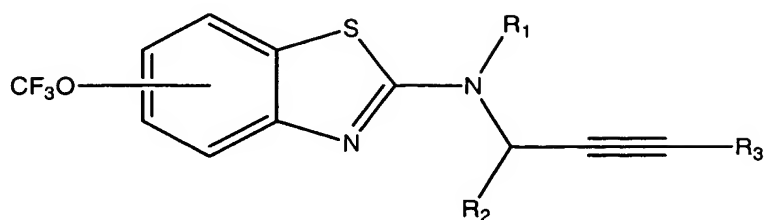


52. (Original) The process of claim 51, wherein the polar solvent is acetonitrile and the base is potassium carbonate.

53. (Original) The process of claim 48, further comprising reacting the product of step (c), wherein R_1 , R_2 and R_3 are each H, with 2-chloroethyl methylsulfide in a polar solvent in the presence of a base, to produce a compound having the structure:



54. (Original) The process of claim 53, wherein the polar solvent is acetonitrile and the base is potassium carbonate.
55. (Original) The process of claim 48, wherein the amine exchanging agent is a mixture of aqueous NH_2NH_2 and hydrazinium sulfate in ethylene glycol.
56. (Original) The process of claim 55, wherein the chlorinating agent is $SOCl_2$.
57. (Original) The process of claim 56, wherein R_1 is C_1 - C_4 alkyl and R_2 and R_3 are H.
58. (Original) The process of claim 48, wherein the alkylating agent in step (d) is methyl iodide or dimethyl sulfate.
59. (Original) A process of manufacturing a compound having the structure:



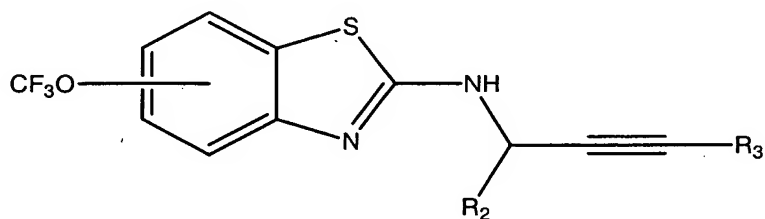
wherein

R₁ is C₁-C₄ alkyl;

R₂ is H or C₁-C₄ alkyl; and

R₃ is H or C₁-C₄ alkyl,

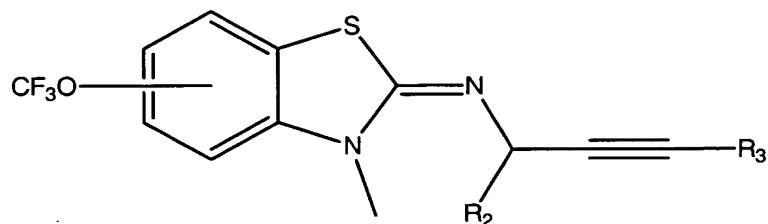
comprising reacting a compound having the structure:



with R₁X in a polar solvent in the presence of a base, wherein X is a halogen atom, to produce the compound.

60. (Original) The process of claim 59, wherein the polar solvent is acetonitrile and the base is potassium carbonate.

61. (Original) A process of manufacturing a compound having the structure:



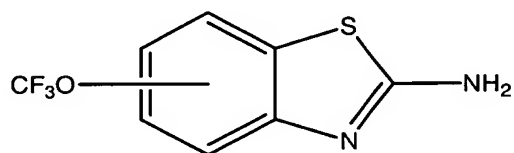
wherein

R₂ is H or C₁-C₄ alkyl; and

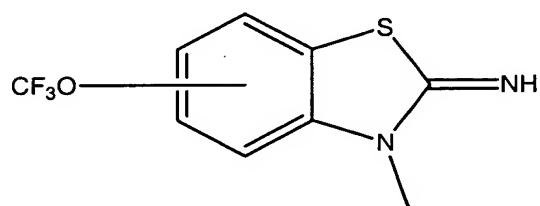
R₃ is H or C₁-C₄ alkyl,

comprising,

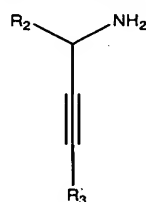
a) reacting



under suitable conditions with a methylating agent, in the presence or absence of solvent to provide:

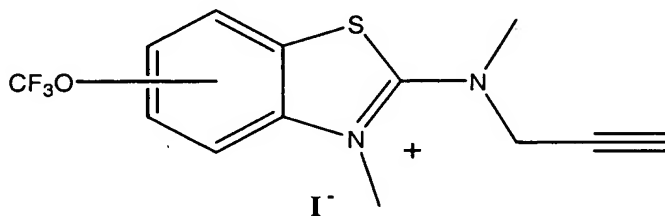


b) reacting the product of step a) with

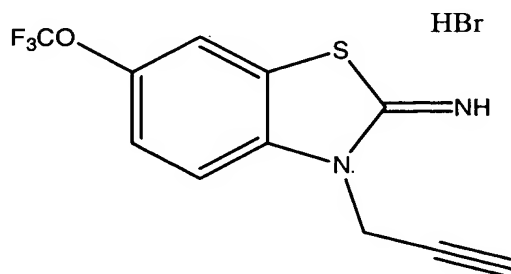


in the presence of p-toluenesulfonic acid to provide the compound.

62. (Original) The process of claim 61, wherein the product of step (b) is further alkylated with an alkylating agent to provide a compound having the structure:

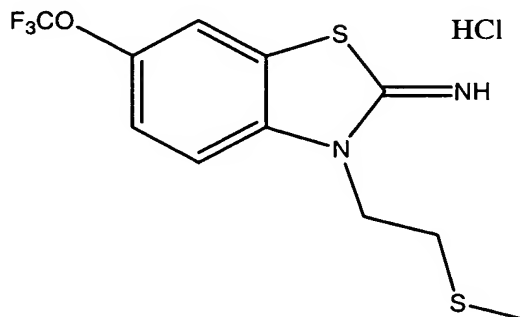


63. (Original) The process of claim 61, wherein the methylating agent in step (a) is methyl iodide or dimethyl sulfate.
64. (Original) The process of claim 62 wherein the methylating agent is methyl iodide.
65. (Original) A process of manufacturing the compound of claim 19 comprising reacting a compound having the structure:



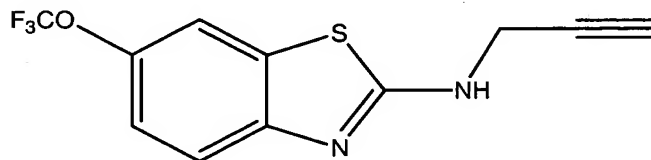
with propargylamine and p-TsOH in toluene to produce the compound.

66. (Original) A process of manufacturing the compound of claim 18 comprising reacting a compound having the structure:

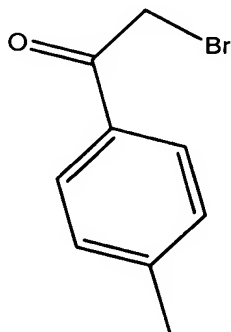


with propargylamine and p-TsOH in toluene to produce the compound.

67. (Original) A process of manufacturing the compound of claim 20 comprising reacting a compound having the structure:



with



in a polar solvent to produce the compound.

68. (Original) The process of claim 67, wherein the polar solvent is acetonitrile.

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Claims 69-73. (Canceled)

74. (New) The method of claim 38 wherein the therapeutically effective amount of the compound is administered by injection, systemically, orally or nasally.